Charles University

Faculty of Pharmacy in Hradec Králové

Department of Pharmacology & Toxicology

Student: Veronika Křečková

Supervisor: PharmDr. Lukáš Červený, Ph.D.

Title of diploma thesis: Role of drug transporters in placental transfer of entecavir

Entecavir (ETV), an analogue of guanosine, is a highly efficient anti-hepatitis B antiviral drug. It is the first-line therapy for both adults and children. Its use in pregnancy is limited due to a number of factors, including lack of data on placental pharmacokinetics. The placental transition of drugs is frequently controlled by drug transporters. ATP-binding (ABC) transporters, P-glycoprotein (P-gp), breast cancer resistance protein (BCRP) or multidrug resistance-associated protein 2 (MRP2) localized in the apical membrane of syncytiotrophoblast and pumping their substrates in the feto-maternal direction belong to most significant determinants of placental pharmacokinetics. Moreover placental transport of nucleoside-derived drugs can be affected by the activity of nucleoside transporters (NTs); equilibrative nucleoside transporters (ENTs) mediate facilitated diffussion, while the concentrative nucleoside transporters (CNTs) control active influx of their substrates.

The aim of the diploma thesis was to describe the role of P-gp, BCRP, MRP2 and NTs (ENTs and CNTs) in placental transfer of ETV. For this purpose, an *in vitro* transport method was performed on MDCKII cells expressing the human P-gp, BCRP or MRP2 and the accumulation method performed using BeWo cell line derived from placental choriocarcinoma. We found that ETV is not a substrate of P-gp, BCRP or MRP2, but we have confirmed that it is a substrate of ENT1. it can be conluded that ENT1 might contribute to ETV placental transfer. Further experiments on more complex models are, however, needed to fully describe the ETV placental pharmacokinetics and the practical application of these findings.